

БИОГЕРОНТОЛОГИЯ

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AGE-RELATED ANDROGEN DEFICIENCY IN MEN AND CARDIOVASCULAR DISEASES

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In last year the very big interest to the problem of androgen deficiency take place (ADAM). The purpose of this study was to examine the VAD men in connection with the development of their cardiovascular disease and subsequent development of clinical and laboratory biochemical criteria to reduce gonadal function in this patient group. The study included 314 patients. The development of cardiovascular disease VAD is starting to influence the age of 40-50 years. Biochemical criteria for VAD in the presence of cardiovascular disease characterized by average levels of total testosterone level 2,28-2,29 ng / ml in serum free testosterone - 60,1-68,1 pg / ml. ADAM in association with cardiovascular diseases, is characterized by symptoms such as general weakness, difficulty in falling asleep and daytime sleepiness, irritability, panic attacks, the formation of sense of " lifelessness", as well as decreased libido, decrease in morning erections, decrease in frequency of sexual activity.

Keywords: androgen deficiency, cardiovascular pathology.

ВОЗРАСТЗАВИСИМЫЙ АНДРОГЕННЫЙ ДЕФИЦИТ У МУЖЧИН И КАРДИОВАСКУЛЯРНЫЕ ЗАБОЛЕВАНИЯ

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В последние годы наблюдается повышенный интерес к проблеме возрастного андрогенного дефицита (ВАД). Цель данного исследования состояла в изучении ВАД у мужчин во взаимосвязи с развитием у них кардиоваскулярной патологии и последующей разработке клинических и лабораторно-биохимических критериев снижения гонадной функции у этой группы пациентов. В исследование было включено 314 пациентов. На развитие сердечно-сосудистой патологии ВАД начинает оказывать влияние в возрасте 40-50 лет. Биохимические критерии ВАД при наличии сердечно-сосудистой патологии характеризуются средними уровнями общего тестостерона на уровне 2,28-2,29 нг/мл в сыворотке крови, свободного тестостерона – 60,1-68,1 пг/мл. ВАД в ассоциации с кардиоваскулярной патологией характеризуется такими симптомами как общая

слабость, утомляемость, сложностью в засыпании, дневной сонливостью, ощущением потери смысла жизни, вкупе со снижением либидо, уменьшением утренней эрекции, степени сексуальной активности.

Ключевые слова: андрогенный дефицит, сердечно-сосудистая патология.

Introduction.

In recent years, much attention is paid to the reproductive health of men in all age groups. This is due to many factors of which increase in male infertility is an example, very much noticed in the general population especially in people with endocrine disorders, disorders that lead to a change in behaviour, and the development of associated somatic and neuropsychiatric diseases [1, 3].

Another important aspect is the immense influence of somatic diseases on the male reproductive system. Not ruling out the high prevalence of harmful habits such as smoking, high alcohol consumption and Many forms of psychoactive substance addiction, which adversely affects the secretory function and homeostasis of the male sex hormones [2, 4, 5, 6].

The actual question of much relevance is the prevalence, early diagnosis and treatment of androgen deficiency in ageing men (ADAM) suffering from the most common group of diseases associated with the cardiovascular system.

The aim is the study of the prevalence of ADAM with concomitant cardiovascular disease and the development of clinical and laboratory-biochemical criteria for the diagnosis in the decrease of male gonadal function in this group of patients.

Materials and methods. The study included 314 patients, 248 (79.0%) of them had no problems of sexual nature and were patients of general practitioners who voluntarily completed the AMS-questionnaire, the remaining patients in this case, 66 men (21%) visited the sexologist with sexual dysfunctions and these Patients were also registered with cardiac dysfunction which included: 1 - 3 stage and 2 - 3 degrees risk of complications – 59 people, 1 - 2 degrees obesity – 41 patients compensated diabetes mellitus- 32 patient. Pro-atherogenic dyslipoproteinemia – 54, metabolic syndrome – 62 people; erectile dysfunction – 66 cases (table 1).

The patients aged from 40 to 70 years, the quantitative category of patients with different age groupings were as follows: 40 - 45 years - 28 patients (8.9%), 46 - 50 years - 35 patients (11,2%), 51 – 55 years – 41 patients (13,1%), 56 - 60years – 37 patients (11,8%), 61 – 65 – 43 patients (13,7%), 66 - 70 years – 47 persons (14,9 %).

Table 1

Age and nosological characteristics of patients used in this study

Age (years)	Nosology (number of patients)						
	BP.	Obesity	Diabetes	dyslipidemia	Erectile dysfunction.	Metabolic syndrome	Total
40 – 45	3	5	3	2	8	7	28
46 – 50	6	6	5	5	7	6	35
51 – 55	9	3	4	8	9	8	41
56 – 60	8	4	5	7	7	6	37
61 – 65	9	4	3	9	9	9	43
66 – 70	24	19	12	23	26	26	130

The Clinical diagnosis of ADAM is based on the "aging male questionnaire", or the AMS-questionnaire. It conceded the following items: general patient conditions; joint-muscle pain, sweating, insomnia, drowsiness, fatigue, irritability, restlessness, panic attacks, impatience; muscle weakness, depression, the feeling of "worthlessness", a feeling of emptiness, low growth of facial hair, decreased libido, decrease in intensity and quality of erections, decrease in performance and number of sexual encounters.

Results interpretation of points: from 0 - complete absence of symptoms, up to 4 - were very symptomatic). Laboratory diagnosis of ADAM were performed using the ELISA method test systems, with the help of a photometer «Multiskan Plus» at a wavelength of 450 nm. The levels of total and free testosterone were determined, these were ranked into three categories - normal, marginal decrease, decrease (table 2).

For the statistical processes of the study results applied, the method of assessing the significance of differences between two sets by applying the criterion of t-Student. The difference in indicators is true when $t \geq 2$, in this case, $p < 0.05$. Student's t criterion is used to identify the main differences between the quantitative characteristics of the study process. During the statistical calculations of the data, values were put into tables using «Excel», mathematical and statistical processing were carried out using the program «Stat graphics plus for Windows», the version 7.0.

Table 2

Ranking the total and free testosterone levels, depending on its degree of reduction in the blood serum

The degree of reduction in fractional testosterone	Total testosterone (ng/ml)	Free testosterone (ng/ml)
Normal contents	>3,46	>72,00
Marginal decrease	2,31 – 3,46	65,00 – 72,00
Pathological decrease	<2,31	<65,00

Results.

According to the survey using a special scale, ADAM was detected in 80.7% of cases. The distribution of patients with ADAM was of uniform nature up to 60 years: 40 - 50 years - 42,0%, 51 - 60 years - 50,0%, 61 - 70 years - 8,0%.

Clinical symptoms of ADAM was of the following character: "decline in general state" $3,3 \pm 0,01$ points, "increase in exhaustion" - $2,8 \pm 0,01$ points, "muscular weakness" - $2,9 \pm 0,02$ points; "depression" - $2,8 \pm 0,02$ points, the sense of "everything in life is behind" - $2,6 \pm 0,01$ points, feeling "empty" - $2,8 \pm 0,01$ points, the "reduce hair growth" - $2,7 \pm 0,02$ points, "reduction in the frequency of sexual intercourse" - $2,9 \pm 0,02$ points, a decrease of "morning erection" - $2,8 \pm 0,02$ points, decrease in "libido" - $2,8 \pm 0,01$ points, $p < 0,05$.

Testosterone levels in different clinical situations were as follows. It was noticed that in the absence of complaints by patients in the sexual sphere the normal values of fractional testosterone were observed in 18.2% cases, marginal values - 81,8%. The content of total testosterone in the latter case was $2,33 \pm 0,2$ ng/ml, free testosterone $4 \pm 5,0$ pg/ml.

In the presence of complaints of sexual nature normal testosterone was noted in 9.1%, marginal level values - 18,2%, a decrease in testosterone serum content - 72,7%.

In the marginal hormonal levels the average values were as follows: total testosterone - $2,35 \pm 0,1$ ng/ml, free testosterone $67,9 \pm 4,5$ pg/ml, in decreased levels: total testosterone - $2,28 \pm 0,2$ ng/ml, free testosterone $64,1 \pm 4,1$ pg/ml (table 3).

Table 3

Testosterone levels in men with metabolic syndrome and sexual dysfunction

Character of decline in testosterone levels	Number of patients	Level of general body testosterone, ng/ml	Level of free testosterone, ng/ml
Normal levels	1 (9,1%)	3,90±0,1	75,9±5,1
Marginal levels	2 (18,2%)	2,35±0,1	67,9±4,5
Reduced levels	8 (72,7%)	2,28±0,2	64,1±4,1

Discussion.

In recent years, considerable attention was paid to polymorbidity and common aggravation of diseases. It is from these positions that we consider the question of progression, diagnosis and treatment of diseases in persons aged 50 years and over. There is no exception to ADAM, which often develops as a result of concomitant somatic and neuropsychiatric diseases.

The effects of somatic and psycho-neurological pathology in ADAM can significantly reduce both the quality of diagnosis of disease and the effectiveness of prevention likewise the treatment programs. It should be noted that, in general, ADAM occurs in persons aged over 50 years, and at this age there is an accumulation of a number of age-related and pathological changes that contribute to the alteration of the disease progress. These features include:

1. There is an overall increase in pathological conditions, when there is a corresponding increasing number of nosological forms, dominated by chronic diseases, characteristic of polymorbidity.

2. Peculiar etiological features in diseases of the elderly: is affected by the internal environmental factors (age-related changes in organ systems, metabolism, and regulation) increases the aggressiveness of pathogens and reduces the resistance of older people.

3. Peculiarity of the pathological Pathogenesis in the middle and old age, quite often changes the specific pathogenic mechanisms of disease.

4. Clinical features of disease in the elderly: the diseases are usually atypical – less symptomatic, latent, diseases masks itself as other diseases and are often very severe, more often disabling, more likely to relapse, and often the transition of acute forms to chronic,

shorten latent period of the disease; leading to frequent complications, reduced time for the development of complications, by increasing the functional decompensation of the affected system, thus the reduction of life expectancy of the patient.

Thus, patients above 50 year of age with cardiovascular disease are prone to the development of ADAM. On the other hand, testosterone deficiency can also causes development of a vicious circle within the cardio-vascular diseases cycle. Therefore the influence of androgens on the cardiovascular system is very significant.

It has been proven that there is a direct effect of androgens on the vascular wall, this entails in the modulation of activity in the potassium channels and stimulating the secretion of nitric oxide. This causes vasodilating effect in the vessels. The Positive effect of testosterone mainly undertaken by estrogen i.e. testosterone because it is a major source of estrogen. Estrogens have direct protective effects on cardiomyocytes. Age associated reduction of the testosterone concentration in turn reduce estrogen, which in turn leads to the the overall reduction of the efficiency of cardio protection.

Androgens have a positive influence on the hemostatic system. This is reflected in its ability to reduce the level of fibrinogen, proconvertin clotting factor VII. at the same time a number of studies have shown that testosterone seems to have pro-aggregation properties due to its ability to decrease the activities of cyclooxygenase and to reduce anti aggregatory properties of prostaglandin

Testosterone, as shown in several studies, has antiatherogenic effects. particulaly, low level of testosterone is associated with a high degree of occlusion of coronary artery. These are the pathogenetic relationship between cardiovascular disease and ADAM. These were confirmed in our studies and put into practice by the development of diagnostic algorithms ADAM for the most common disease of the heart and blood vessels.

Conclusion.

In the study of cardiovascular disease ADAM occurs from the age of 40 – 50 years. ADAM in association with cardiovascular diseases, is characterized by symptoms such as general weakness, difficulty in falling asleep and daytime sleepiness, irritability, panic attacks, the formation of sense of "lifelessness", as well as decreased libido, decrease in morning erections, decrease in frequency of sexual activity. Biochemical characteristics of ADAM in the presence of cardiovascular disease is

the average level of total testosterone within the range 2.28 - 2.29 ng / ml, free testosterone - 60,1 - 68,1 pg / ml.

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